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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/469,485	12/22/1999	QINJIAN ZHAO	20369Y	5022

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EXAMINER
FOLEY, SHANON A

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/469,485	ZHAO ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 December 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group II in Paper No. 8 is acknowledged. The traversal is on the ground(s) that the Office has failed to demonstrate that an rHBsAg made by other recombinant techniques retains the same specific antigenicity recited in the claims.

Applicant's arguments have been fully considered, but are found unpersuasive because the instant claims are not drawn to "specific antigenicity". Claims 1-4 recite, "relative potency", which is different from "specific antigenicity". It is presumed that applicant intended "relative potency" in the rebuttal since this phrase is what is recited in the claims, so the response to the traversal will be directed at this phrase. The term "relative potency" is vague and indefinite and is not defined in the disclosure. It cannot be determined what is intended by "potency" and the degree of strength also cannot be determined because it is "relative". Therefore, since it cannot be determined what is intended by this limitation, any rHBsAg produced by any recombinant means would inherently possess properties recited in the claims.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-7 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8. Claims 8-20 are under consideration.

Sequence Compliance

The specification is objected to for failing to adhere to the requirements of the sequence rules. Applicant must append SEQ ID Nos. to all mentions of specific sequences in the specification, i.e., Figure 3. See 37 CFR § 1.821 (a)-(d) and MPEP § 2422.

Drawings

The drawings are objected to because the text at the top is hard to read in Figure 2 and the lines and sample labels in the are illegible, especially in the second graph. The graphs in Figure 2 should be labeled "2A" and "2B" to be consistent with the specification on page 4, lines 21-28 and page 24, lines 27-30. The sequences in Figure 3 is are very hard to read and are illegible in some places. The text in Figures 5 and 7 is illegible. Also, Figure 6 is uninterpretable because it cannot be determined what "A", "B" and "C" represent in the X-axis of Figure 6. There is also no mention of what "A", "B" and "C" represent in the brief description on page 5, lines 1-2. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. Applicant is reminded that no new matter may be introduced into the disclosure. The objection to the drawings will not be held in abeyance.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 8-20 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 8-20 of copending Application No. 09/869007. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is rejected because it cannot be determined what temperatures and hours are encompasses by "about". Step c is drawn to adjusting the temperature from 34°C to 38°C, but the previous steps do not indicate that the temperature is 34°C when the steps are performed. Therefore, how can a temperature be adjusted (increased) from 34°C to 38°C if steps a and b are not at 34°C? In addition, if the temperature is adjusted from 34°C to 38°C in step c, is the temperature adjusted back down to 34°C before performing step d? Also, there is no step directed to meeting the requirements of the preamble in the claim. This rejection affects all dependent claims.

Claim 9 states that step c is performed before step b, but step b does not specify that the temperature is 34°C.

Claim 10 is vague and indefinite for reciting "less than about" in line 3. Also, the claim is unclear because it cannot be determined what compounds are encompassed by the "corresponding disulfide compounds".

Claims 12-14, 16, 18 and 20 are indefinite for reciting "about". The metes and bounds of the ratio proportions, concentrations, and hours cannot be determined.

Claim 14 recites the limitation "glutathione to oxidized glutathione" in line 2. There is insufficient antecedent basis for this limitation in the claim. It is presumed that "glutathioné" is intended to be the thiol compound in claim 13. If this presumption is correct, it is suggested that applicant amend the claims to have claim 14 depend from claim 15.

Claim 18 is confusing because the step c of claim 8 specifies that the temperature is adjusted from 34°C to 38°C and step f of claim 18 is drawn to incubating rHBsAg at 34°C. Is the temperature readjusted back to 34°C before step f of claim 18?

Claim 19 depends from claim 17 and is unclear. Claim 17 comprises two steps, adding an aluminum adjuvant and co-precipitating the rHBsAg and the adjuvant. These steps are followed by claim 19, which comprises adding an aluminum adjuvant and co-precipitating the rHBsAg and the adjuvant. Does applicant intend for the steps of claim 17 to be repeated?

Claim 20 recites the limitation "step d" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8-16 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable Builder et al. (US 4,620,948).

The claims are drawn to a method of making a recombinant hepatitis B surface antigen (HbsAg) by obtaining a sterile filtered rHBsAg from cell culture, adding a redox buffer comprising glutathione and oxidative glutathione, incubating the buffer and antigen at a temperature between 34°C to 38°C.

Builder et al. teaches a method of purifying various proteins by isolating protein from cell cultures, adding 10mM GSH: 1mM GSSG, and incubating mixture overnight, see examples 13 and 14. Although Builder et al. does not teach incubation at an elevated temperature in the specific examples, the reference teaches that optimal incubation temperatures range from 0°C to 37°C, see column 16, lines 29-55.

Although Builder et al. does not explicitly teach purifying HbsAg with the method, one of ordinary skill in the art at the time the invention was made would have been motivated to use the method of Builder et al. to ensure proper protein folding and increase the protein yield obtained by eliminating refractile bodies, see column 1, lines 9-68. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation in producing the claimed invention because Builder et al. teaches HbsAg is conventionally produced by cell culture, see Builder et al. column 1, lines 9-68, which result in insoluble refractile bodies and the reference teaches a method of freeing recombinant proteins from refractile bodies. Therefore, the invention as a whole would have bee prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Claims 17 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Builder et al. as applied to claims 8-16 and 20 above, and further in view of Petre et al. (WO 93/24148 A1).

The clams are drawn to adding an aluminum hydroxide adjuvant after the method steps of claim 8 and co-precipitating rHBsAg and the adjuvant.

See the teachings of Builder et al. above. The reference does not teach adding an aluminum hydroxide adjuvant and co-precipitating the antigen and the adjuvant.

However, Petre et al. teaches a method of adsorbing rHBsAg on an aluminum hydroxide adjuvant, see claims 26 and 27.

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the rHBsAg purified by the method of Builder et al. with the aluminum hydroxide adjuvant of Petre et al. to enhance the immunogenicity of the antigen and make an effective vaccine, see claims 1 and 4 of Petre et al. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation in producing the claimed invention because the antigen of Builder et al. would be available in large quantities and the method would ensure that the antigen in properly folded for correct immunologic presentation to the immune system. One of ordinary skill would have had a further reason to expect success because Petre et al. teaches that the vaccine composition comprising the adjuvant and the rHBsAg is stable at 37°C for a week, which is the incubation temperature in the method of purifying rHBsAg in the method of Builder et al. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Builder et al. as applied to claims 8-16 and 20 above, and further in view of Even-Chen (US 5,242,812)

The claim is drawn to adding formalin and incubating the rHBsAg at 34°C to 38°C for 40 to 72 hours in addition to the method steps of Builder et al.

See the teachings of Builder et al. above. The reference does not teach the method steps of claim 18.

However, Even-Chen teaches that formalin treatment of HbsAg is necessary to make the product safe for human use, see column 3, lines 59-60.

One of ordinary skill in the art at the time the invention was made would have been motivated to formalin-treat the rHbsAg of Builder et al. to render the product safe for human consumption. One of ordinary skill in the art would have had a reasonable expectation for producing the claimed invention because Builder et all teaches a method of purifying antigens with a method to maintain proper folding and Even-Chen teaches that formalin is added after the rHBsAG has been purified. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention as made, absent unexpected results.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SAF

Shanon Foley/SAF
June 23, 2002

James C. Housel

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